Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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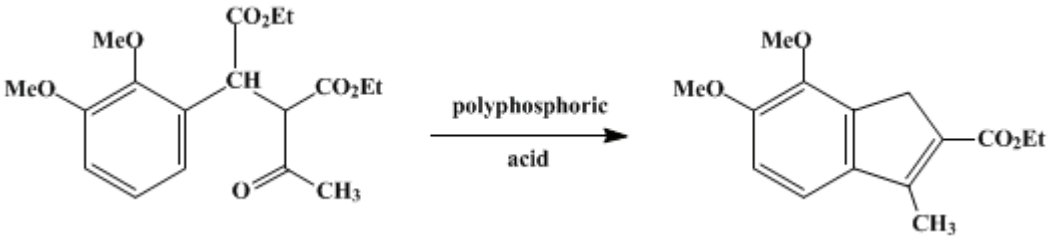
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.040.0043

Organic Syntheses, Coll. Vol. 5, p.550 (1973); Vol. 40, p.43 (1960).

ETHYL 6,7-DIMETHOXY-3-METHYLINDENE-2-CARBOXYLATE

[Indene, 6,7-dimethoxy-3-methyl-2-carbethoxy-]



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Checked by John C. Sheehan and J. Iannicelli.

1. Procedure

To 300 g. of polyphosphoric acid (Note 1) precooled to 5° is added 28 g. (0.1 mole) of ethyl α-acetyl-β-(2,3-dimethoxyphenyl)-propionate[2] contained in a 400-ml. beaker. The mixture is stirred thoroughly (Note 2) with a strong spatula for 15 minutes. The temperature, which is around 10° at the beginning, increases rapidly and is kept between 20° and 25° by occasionally cooling the beaker in an ice-water bath (Note 3). The deep-yellow reaction paste is then poured immediately into 600 ml. of ice water with thorough stirring and trituration (Note 4), and the beaker is rinsed with small portions of cold water. The product, which separates from the cold water as a colorless precipitate, is extracted with several portions of chloroform (first with 400 ml., then twice with 200 ml., and finally with 100 ml. of this solvent). The combined chloroform extracts are washed successively with 100 ml. of cold water, then once with 100 ml., twice with 50 ml. of 10% sodium bicarbonate solution (Note 5), and finally with 50 ml. of cold water. The chloroform solution is dried over magnesium sulfate and filtered. The chloroform is removed by distillation on a steam bath first at atmospheric pressure and finally under reduced pressure. The residual pale-yellow oil soon solidifies and is practically pure. The yield of ethyl 6,7-dimethoxy-3-methylindene-2-carboxylate is 21.5–22.5 g. (82–86%), m.p. 81–83° (Note 6).

2. Notes

1. Obtained from Victor Chemical Works, Chicago, Illinois.
2. Since the mixture is so viscous, continuous and vigorous hand stirring is necessary.
3. After the reaction starts, the temperature should be checked every few minutes and kept between 20° and 25°, which is the most favorable temperature.
4. Careful stirring and trituration are necessary to ensure the complete decomposition of every drop of the yellow paste.
5. According to the submitter, acidification of the combined sodium bicarbonate washings with 10% hydrochloric acid yields a colorless precipitate of 6,7-dimethoxy-3-methylindene-2-carboxylic acid, which is collected by filtration, washed, and dried; yield, 3.4–3.9 g. (14–16%); m.p. 216–218°.
6. Recrystallization from 75 ml. of 60% ethanol gives a 90% recovery of colorless long needles, m.p. 83–85°.

3. Discussion

The method described here is based on the analogous preparation of some other indenes.[3]

References and Notes

1. Present address: National Drug Company, Research Laboratories, Philadelphia, Pennsylvania.

Work done in the Laboratory of Chemical Pharmacology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.
2. E. C. Horning, J. Koo, M. S. Fish, and G. N. Walker, *Org. Syntheses*, Coll. Vol. **4**, 408 (1963).
3. J. Koo, *J. Am. Chem. Soc.*, **75**, 1891 (1953).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

polyphosphoric acid

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

magnesium sulfate (7487-88-9)

ETHYL α-ACETYL-β-(2,3-DIMETHOXYPHENYL)-PROPIONATE (53608-80-3)

Ethyl 6,7-dimethoxy-3-methylindene-2-carboxylate,
Indene, 6,7-dimethoxy-3-methyl-2-carbethoxy- (5415-54-3)

6,7-dimethoxy-3-methylindene-2-carboxylic acid